A. Double Patenting Rejection addressed

The provisional rejection of claims 1-34 is maintained. A terminal disclaimer will be filed with respect to the '189 application when patentable subject matter has been determined.

B. Section 112, first paragraph rejections addressed

Claims 1-9, 11-22, and 24-33 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, has possession of the claimed invention. The Office Action states that the limitation "0.2-30% by volume" recited in claims 1 and 21 as currently pending is not supported by the originally filed specification or claims.

Claims 1 and 21 have been amended herein to replace the amount of alcohol from "0.2 - 30% by volume" to "0.2 - 13% by volume," thereby obviating this rejection. Support for this amendment can be found in the disclosure in paragraphs [0049] and [0051]. Withdrawal of this Section 112, first paragraph rejection is requested.

C. Section 112, second paragraph rejections addressed

Claims 1-33 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite. The Office Action states that the expression "sufficient amount of an acid to adjust the pH" in claims 1 and 21 renders the claims indefinite as to what amount of acid is encompassed by the claims. This rejection is respectfully traversed.

It is asserted that it is not necessary to recite the specific amount of acid required in each of the claimed compositions. Rather, all that is required is that a sufficient amount of the acid be added until the pH of the composition is between 2.45 and 4.6. It is well within the skill of persons skilled in the art to measure the pH of a solution (e.g., with a pH meter) during or after the addition of an acid to the solution and to make a determination as to whether the pH of the solution is between 2.45 and 4.6. It is asserted that pending claims 1-33 are clear and definite, and withdrawal of this rejection is requested.

D. Section 103(a) Rejections addressed

1. Claims 1-6 and 9-34 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Yu et al. in view of Poli *et al.* and Wenniger.

This rejection is respectfully traversed.

To establish a *prima facie* case of obviousness, it is well established that the prior art reference or combination of references must teach or suggest all the limitations of the claims. It is asserted that this burden has not been met by the Office Action and therefore a *prima facie* case of obviousness has not been established.

Claims 10 and 23 have been cancelled herein, and independent claims 1 and 21 have been amended to further distinguish the claims over the cited art. More specifically, independent claim 1 has been amended to recite a method of treating an inflammation or lesion caused by a virus, comprising contacting said inflammation or lesion with a virucidally effective amount of a composition **comprising** a synergistic combination, said synergistic combination **consisting essentially of**:

- 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol and
- a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.

Independent claims 21 and 34 have been similarly amended. It is asserted that this amendment, which without question distinctly points out the novel, active component of the inventive composition, clearly distinguishes claim 1 over the cited art.

More specifically, the courts have ruled that when the phrase "consisting of" appears in a clause of the body of a claim rather than immediately following the preamble, it limits only that element set forth in that claim; the courts have declined to read this usage of "consisting of" as excluding all other elements from the claim as a whole. *Mannesmann Demag Corp. v. Engineered Metal Products Co.*, 793 R.2d 1279, 230 USPQ 45 (Fed. Cir. 1986). The term "comprising" implies that the **composition** can include other ingredients, such as fillers, etc. commonly used in formulating pharmaceutical compositions. Thus, the amendment to claim 1 clearly indicates that any element or ingredient other than 0.2-13.0% by volume of a C1-C3 alcohol or a C2-C4 diol and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6 is excluded from the effective synergistic combination of claim 1. However, the inventors are certainly entitled to include nonacitve ingredients such as ointment, cream fillers, solvents, etc. in a formulation comprising this synergistic combination, and the transitional phrase "comprising" after the term "topical composition" allows for the addition of such ingredients. It would clearly undermine the entire patent process to allow a third party to make unimportant, insubstantial changes and

substitutions to the synergistic combination of claim 1 in order to be able to circumvent the present invention by not allowing the language as provided in amended claim 1.

In contrast, Yu teaches a first example of composition containing two agents: an alpha hydroxyacid or alpha ketoacid and an amphoteric or pseudoamphoteric compound. The amphoteric or pseudoamphoteric compound is intentionally added to raise the pH of the composition in order to avoid skin irritation (see column 4, lines 2-12). Specifically, Yu states that a 1 molar aqueous solution of glycolic acid has a pH of 1.9, but the pH of the composition changes to 3.0 or 3.2 when an amphoteric compound such as arginine or creatinine, respectively, is combined with the glycolic acid solution. Thus, in this example Yu's active composition requires both an alpha hydroxyacid and an amphoteric compound. Therefore Yu's composition contains an element, i.e., an amphoteric compound, which is specifically excluded from the elements allowed in the synergistic combination of claim 1.

Yu also describes a formulation containing specific alpha hydroxy acids which are therapeutically effective for certain skin disorders without utilizing an amphoteric system (column 11, line 55-column 12, line 2), and provides glycolic acid as an example of an effective alpha hydroxy acid. However, as discussed above, the pH of a glycolic acid solution that does not include an amphoteric compound is **1.9**, which is outside of the pH range of 2.45 to 4.6 as required in claim 1. Accordingly, this alternative composition disclosed by Yu is also outside of the scope of amended claim 1.

Therefore, since Yu does not teach every element of the composition of claim 1, Yu cannot render claim 1 obvious. For the same reasons, Yu also does not teach every element of claims 2-6 and 9-34, and therefore claims 2-6, 9, 11-22 and 24-34 are also nonobvious in light of Yu.

Next, the Office Action states that while Yu does not expressly teach that 1,3-butanediol is useful as a pharmaceutical vehicle, Wenniger teaches that 1,3-butanediol is useful as a solvent in numerous cosmetic marketed products. However, it is asserted that the Wenniger reference adds nothing to Yu that would render claims 1-6 and 9-33 obvious. Even if there were a motivation to combine the references, the combination would not provide a method of treating an inflammation or lesion caused by a virus by contacting the inflammation or lesion with a composition **comprising** a synergistic combination, said synergistic combination **consisting essentially of** 0.2-13% by volume of a C1-C3 alcohol or a

C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.

For the reasons presented above, the compositions of the present invention, considered as a whole as required by Section 103, would not have been *prima facie* obvious to one skilled in the art at the time this invention was made. None of the cited reference, alone or in combination, teach or suggest the compositions of claims 1-6, 9, 11-22, and 24-34. Accordingly, withdrawal of the obviousness rejection of claims 1-6, 9, 11-22, and 24-34 is respectfully requested.

2. Claims 1 and 7-8 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Bhatia et al. in view of the article entitled "Disinfectant Drugs" and Remington. The Office Action states that while Bhatia et al. teach that 0.4 N hydrochloric acid is effective in inactivating sheep pox virus, they do not teach the use of hydrochloric acid with an alcohol, however the "Disinfectant Drugs" article teaches isopropanol at concentrations of 15% or above is effective as a single medicinal ingredient for disinfecting contact lenses, and Remington teaches that isopropanol and ethanol are very good pharmaceutical solvents. The Office Action then concludes one skilled in the art would have been obvious to combine the cited art because isopropanol is known to be useful as both a solvent and a disinfectant and hydrochloric acid is known to have virucidal activities against pox viruses.

The Office Action's position represents hindsight reconstruction or, at best, establishes it would have been "obvious to try." However, it is well established that "obvious to try" is not the standard in determining obviousness under Section 103(a). Without some suggestion or incentive in the prior art references, independent of the hindsight provided by applicants' claims, it is improper to combine the prior art references in a manner necessary to show applicants' invention in a 35 U.S.C. § 103 obviousness rejection. *In re Samour*, 197 USPQ 1 (CCPA 1978); *In re Rinehart*, 189 USPQ 143 (CCPA 1976). Furthermore, "using an applicant's disclosure as a blueprint to reconstruct the claimed invention from isolated pieces of the prior art contravenes the statutory mandate of section 103 of judging obviousness at the point in time when the invention was made. *Grain Processing Corp v. American Maize-Prods.Co.* 840 F.2d 902, 907 5 USPQ2d 1788, 1792 (Fed. Cir. 1988).

It is asserted that the Examiner has only supplied references that appear to separately contain elements of the claimed invention without pointing to any motivation or suggestion in

the references that they be combined. Furthermore, as discussed below, even if there were motivation to combine the cited references, the combination would not provide the method of the claimed invention.

First, Bhatia only discloses a method of combining goat-pox virus with hydrochloric acid and incubating this suspension for a period of time (see page 518, second column, last paragraph). In order to determine if the virus was still active after incubation with acid, Bhatia injected the suspension under the goats' skin and watched for signs of pain at the injection site. Thus, the Bhatia composition is actually a mixture of the goat-pox virus and a concentrated acid. However, Bhatia does not teach or even suggest combining the acid/goat pox mixture with an alcohol, let alone a method of treating an inflammation or lesion caused by a virus by applying to the inflammation or lesion a composition **comprising** a synergistic combination, said synergistic combination **consisting essentially of** 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6. Accordingly, there is no motivation to combine the teachings of Bhatia with the other cited references.

Next, even if there were motivation supplied in Bhatia to combine the teachings in the "Disinfectant Drugs" article (which there is not), the combination still would not provide the method of the claimed invention. As discussed above, the claims as amended herein are directed to a method of treating an inflammation or lesion caused by a virus by contacting the inflammation or lesion with a composition **comprising** a synergistic combination, said synergistic combination **consisting essentially of** 0.2-13% by volume of a C1-C3 alcohol or a C2-C4 diol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6. In contrast, the cited article only discloses isopropanol at a concentration greater than or equal to 15%. Further, the article does not specifically teach that the isopropanol is inactivating viruses. Accordingly, it is asserted that the combination of Bhatia and the cited article would not provide the method of the claimed invention.

Finally, Remington only teaches that ethanol and isopropanol are useful pharmaceutical solvents. However, as stated in the 6th paragraph, 1st column on page 219 of Remington, isopropanol has an advantage over ethanol in that isopropanol contains "not over 1% ethanol, while ethyl alcohol contains about 5% water, often a disadvantage." Thus, Remington teaches away from using between about 0.2 and 13% by volume of a C1-C3 alcohol or C2-C4 diol. For the reasons stated above, it is asserted that a *prima facie* case of

obviousness has not been made, and withdrawal of this rejection over claims 1 and 7-8 is respectfully requested.

CONCLUSIONS

All of the remarks in the final Office Action have been addressed, claims 1-9, 11-22, and 24-34 are believed to be in condition for allowance, and such action is respectfully requested. The fee for filing a Petition for a three month time extension is included with this response. Should any additional fees be due, the Examiner is authorized to charge any fee deficiency associated with this response to Deposit Account No. 50-1123. The Examiner is asked to kindly contact the undersigned by telephone should any outstanding issues remain.

Respectfully submitted,

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COMPLETE SET OF PENDING CLAIMS

Following is a complete set of pending claims 1-9, 11-22, and 24-34, showing amendments made to claims 1, 9, 21, 24, 25 and 34.

B1

1. (Currently amended) A method for treating an inflammation or lesion <u>on a human or animal in need of said treatment, wherein said inflammation or lesion is</u> caused by a virus, comprising contacting said inflammation or lesion with a virucidally effective amount of a composition <u>comprising a synergistic combination, said synergistic combination</u> consisting essentially of 0.2 to ~~30~~ <u>12.5</u>% by volume of a C1, a C2, or a C3 alcohol or a C2, C3, or C4 diol and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6.
2. (Original) The method of claim 1, wherein said alcohol is selected from the group consisting of methanol, ethanol, 1-propanol, and 2-propanol.
3. (Original) The method of claim 1, wherein said alcohol is selected from the group consisting of 2,3-butanediol, 1,2-butanediol, 1,3-butanediol, and 1,4-butanediol.
4. (Original) The method of claim 2, wherein said alcohol is ethanol.
5. (Original) The method of claim 1, wherein said acid is an organic acid.
6. (Original) The method of claim 5, wherein said organic acid selected from the group consisting of glycolic acid, lactic acid, succinic acid, malic acid, citric acid and acetic acid.
7. (Original) The method of claim 1, wherein said acid is an inorganic acid.
8. (Original) The method of claim 7, wherein said acid is hydrochloric acid.
9. (Currently amended) The method of claim 1, wherein the pH of said ~~composition~~ <u>synergistic combination</u> is 2.45.
10. Cancel
11. (Original) The method of claim 1, wherein said virus resides in the dermis or epidermis of a human or animal infected by said virus.
12. (Original) The method of claim 1, wherein said composition is applied topically to reduce or inhibit lesions in an animal or human suffering from an infection by said virus.

13. (Original) The method of claim 1, wherein said virus is a member of the Herpesviridae family.

14. (Original) The method of claim 13, wherein said virus is herpes simplex 1.

15. (Original) The method of claim 13, wherein said virus is herpes simplex 2.

16. (Original) The method of claim 1, wherein said virus is Varicella-zoster virus.

17. (Original) The method of claim 1, wherein said virus is a member of the Poxviridae family.

B1 cont

18. (Original) The method of claim 17, wherein said virus is molluscum contagiosum.

19. (Original) The method of claim 1, wherein said virus is selected from the group consisting of rhinoviruses, adenoviruses, enteroviruses, cornoviruses, respiratory syncytial viruses, influenza viruses and parainfluenza viruses.

20. (Original) The method of claim 1, wherein said composition is a preparation selected from the group consisting of a tincture, gel, ointment, cream, salve, lotion, lip balm, foam, spray and aerosol.

21. (Currently amended) A method for treating an inflammation or lesion caused by a virus, comprising contacting said inflammation or lesion with a virucidally effective amount of a composition consisting essentially of 0.2 to ~~30~~ 12.5% by volume of an alcohol selected from the group consisting of methanol, ethanol, 1-propanol, 2-propanol, 2,3-butanediol, 1,2-butanediol, 1,3-butanediol, and 1,4-butanediol, and a sufficient amount of an acid to adjust the pH of the composition to between 2.45 and 4.6, wherein said acid selected from the group consisting of glycolic acid, lactic acid, succinic acid, malic acid, citric acid, acetic acid, and hydrochloric acid.

22. (Original) The method of claim 21, wherein the pH of said composition is 2.45.

23. Cancel

24. (Currently amended) The method of claim 21, wherein said composition is applied topically to reduce or inhibit lesions in ~~an~~ said animal or human ~~suffering from an infection by said virus~~.

25. (Currently amended) The method of claim 21, wherein said virus resides in the dermis or epidermis of ~~a~~ said human or animal ~~infected by said virus~~.

26. (Original) The method of claim 21, wherein said virus is a member of the Herpesviridae family.

27. (Original) The method of claim 26, wherein said virus is herpes simplex 1.

28. (Original) The method of claim 26, wherein said virus is herpes simplex 2.

29. (Original) The method of claim 26, wherein said virus is Varicella-zoster virus.

30. (Original) The method of claim 21, wherein said virus is a member of the Poxviridae family.

B1 Contd

31. (Original) The method of claim 30, wherein said virus is molluscum contagiosum.

32. (Original) The method of claim 21, wherein said virus is selected from the group consisting of rhinoviruses, adenoviruses, enteroviruses, cornoviruses, respiratory syncytial viruses, influenza viruses and parainfluenza viruses.

33. (Original) The method of claim 21, wherein said composition is a topical preparation selected from the group consisting of a tincture, gel, ointment, cream, salve, lotion, lip balm, foam, spray and aerosol.

34. (Currently amended) A method for treating an inflammation or lesion caused by herpesvirus, comprising topically applying to said inflammation or lesion a composition comprising a synergistic combination, said synergistic combination consisting essentially of 10% by volume ethanol and 0.6% by weight glycolic acid, wherein the pH of the composition is about 2.45.